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EXAMINER	
CHO, DAN SUNG C	

ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
06/07/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/786,518	GREINWALD ET AL.	
	Examiner	Art Unit	
	Dan-Sung C. Cho	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-24* is/are pending in the application.

4a) Of the above claim(s) *24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/8/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

1. Currently, claims 17-24 are pending. Applicant's newly added claim 24 in a paper filed on 2/20/2007 is acknowledged. Newly submitted claim 24 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The applicant elected claims 17-23, drawn to a kit or a microarray and further elected the combination of genetic sequences CDH23, MYO7A, OTOF, SLC26A4 and USH2A, on the papers filed on 8/7/2006, without traverse. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 24 is withdrawn from consideration as being directed to a non-elected invention GJB2. See 37 CFR 1.142(b) and MPEP § 821.03. The restriction requirement was made FINAL on the paper mailed on 10/20/2006. Therefore, claim 24 is withdrawn as drawn to non-elected subject matter.

All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance.

Rejections withdrawn

2. Rejection of claims 17-20 under 35 USC 102 (b) is withdrawn in light of applicant's response filed on 2/20/2007. All other rejections are maintained.

The following rejections are reiterated. Response to Applicant's arguments follows.

Rejections maintained

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 17-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Williamson et al. (Williamson, R., Curator, Deafness Gene Mutation Database, URL: http://hearing.harvard.edu/db/genelist.htm, last updated 9/18/2002) in view of Guo et al., (Guo et at., 2002, Oligonucleotide Arrays for High-Throughput SNPs Detection in the MHC Class I Genes: HLA-B as a Model System, Genome Res., Vol. 12: 447-457).

Williamson teaches Deafness Gene Mutation Database that lists data and links for many of the known genes, mutations and their exon locations for hereditary hearing

impairment. The current list, which was last updated on 9/18/2002, includes CDH23, MYO7A, OTOF, SLC26A4 and USH2A. Williamson teaches, for example, multiple SNPs on USH2A that are associated with Usher Syndrome, a hereditary hearing impairment characterized by having symptoms of hearing impairment and retinitis pigmentosa. The MYO7A mutations are on exons 2, 3, 4, 5, 7, 8, 9, 11, 13, 14, 16, 17, 21, 22, 23, 25, 28, 29, 30, 31, 35, 36, 37, 38, 39, 10, 41, 44, 45, 46, 47-49, 48, 49; USH2A mutations on exons 2, 3, 4, 6, 7, 9, 10, 11, 12, 13, 14, 18, 20, and 21; and OTOF on 8/9, 15, 16, 18, 39, and 48.

With regard to claim 17, reciting "A diagnostic hearing loss microarray comprising at least 5 sequences that are indicative of presence or absence of an allele associated with a risk for hearing loss", Williamson does not teach an array.

With regard to claim 18, reciting "multiple adjacent exons", Williamson does not teach an array with elements comprising of multiple adjacent exons.

With regard to claim 19, reciting "multiple adjacent exons are selected from the group comprising CDH23 exons 2-3, CDH23 exons 4-6, CDH23 exons 7-9, CDH23 exons 10-11, CDH23 exons 12-13, CDH23 exons 14-16, CDH23 exons 17-21, CDH23 exons 22-27, CDH23 exons 28-31, CDH23 exons 32-36, CDH23 exons 37-43, CDH23 exons 44-46, CDH23 exons 47-53, CDH23 exons 53-68, MYO7A exons 5-14, MYO7A exons 16-21, MYO7A exons 16-18, MYO7A exons 22-26, MYO7A exons 28-35, MYO7A exons 36-44, MYO7A exons 45-49, OTOF exons 4-5, OTOF exons 6-8, OTOF exons 9-11, OTOF exons 12-25, OTOF exons 16-25, OTOF exons 16-18, OTOF exons 16-20, OTOF exons 19-20, OTOF exons 21-25, OTOF exons 16-39, OTOF exons 26-

39, OTOF exons 40-47, SLC26A4 exons 1-3, SLC26A4 exons 4-6, SLC26A4 exons 11-18, SLC26A4 exons 19-21, USH2A exons 1-3, USH2A exons 5-9, USH2A exons 10-11, USH2A exons 12-13, USH2A exons 15-16 and USH2A exons 17-20", Williamson does not teach an array with elements comprising of multiple adjacent exons recited in the claim.

With regard to claim 20, reciting "said sequences comprise a single exon", Williamson does not teach an array with elements comprising of a single exon.

With regard to Claim 21, reciting "The microarray of Claim 20, wherein said single exon is selected from the group consisting of MYO7A exon 1 MYO7A exon 2, MYO7A exon 3, MYO7A exon 4, MYO7A exon 15, MYO7A exon 21, MYO7A exon 27, OTOF exon 1, OTOF exon 2, OTOF exon 3, USH2A exon 4, USH2A exon 14 and USH2A exon 21", Williamson does not specifically teach a diagnostic hearing loss microarray with recited individual single exon.

With regard to Claim 22, reciting "A kit for detecting a candidate gene responsible for hearing loss a microarray", Williamson does not teach a diagnostic hearing loss microarray.

With regard to Claim 23, reciting "The kit of Claim 22, wherein the microarray comprises a solid support ...", Williamson does not teach a microarray.

However, Guo teaches exon-specific array with 68 oligonucleotide probes for polymorphisms in exon 2 and 69 for the adjacent exon 3 of human major histocompatibility complex (MHC) using HLA-B as a model system (page 448, left column, paragraph 2). Probes are further grouped into 15 regions for exon 2 and

13 regions for exon 3 (Table 1). Guo teaches further that the exon-specific probes provide unambiguous detection of complex heterozygous SNP combinations (Abstract) in a blind genotype study with 100 samples where correct interpretation of the array hybridization patterns are made for all three homozygous samples and all 97 heterozygous samples (page 455, left column, lines 6-14). Guo teaches solid-support (page 456, left column, paragraph 2), capture probe (page 456, left column, paragraph 2) and hybridization (page 456, right column, Hybridization Conditions). Guo teaches therefore use of exon specific array that can detect single exon as each probe is specific to a SNP in either exon 2 or 3 (page 448, left column, paragraph 2), and simultaneous detection of two ad

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention was made to detect SNPs relevant to a human hearing loss associated genes and mutations taught by Williamson by adapting the simultaneous detection of such SNPs in an exon specific array format taught by Guo. Because the instant application and Guo are drawn to same method, namely a method for discriminating multiple human alleles relevant to a human disorder, one of ordinary skill in the art would have been motivated to adapt the exon-specific array for SNP genotyping of hearing loss-related genes. Guo in that oligonucleotide arrays "afford a much higher throughput, by virtue of parallel analysis of multiple genetic regions" (page 455, left column, first paragraph in Discussion); and "a cost-effective approach for high-throughput polymorphism analysis" (page 447, right column, paragraph 1). Therefore the skilled artisan would have been motivated to have polymorphism taught by

Williamson arrayed in a single array for cost effective and high throughput analysis, simultaneously detecting multiple SNPs associated with a human hearing loss.

Response to Arguments

5. The response traverses the rejection. Applicant's arguments filed 2/20/2007 have been fully considered but they are not deemed persuasive. The response asserts on page 8, para 1 that the Examiner has relied on the Applicant's disclosure for the combination of Williamson and Guo. The response further asserts that that the examiner has provided with no clear and particular evidence that there is motivation to combine the two teachings for a diagnostic hearing loss microarray or a kit comprising the sequences claimed.

This argument has been thoroughly reviewed but was not found persuasive. First, the office action mailed on 10/20/2006, sets forth that Williamson teaches Deafness Gene Mutation Database that lists data and links for many of the known genes, mutations and their exon locations for hereditary hearing impairment. Therefore Williamson teaches gene, mutations, and exons of the genes that are known to be found associated with hearing loss at the time of 9/18/2002. Office action also sets forth clearly that Guo teaches a method of discriminating multiple alleles relevant to human HLA phenotype with regard to HLA alleles (page 447, right col., para 3, lines 1-9) one of ordinary skill in the art would have been motivated to determine hearing loss-related genes that are exon-specific Williamson teaches for cost effective and high throughput

analysis, simultaneously detecting multiple SNPs associated with a human hearing loss on an array format Guo teaches. Because Williamson teaches genes and mutations and exons of the genes and SNP that are associated with hearing loss, one of ordinary skill in the art at the time of the invention was made would want to detect theses genes, mutations and SNPs KNOWN to be associated with hearing loss. Determination of whether a person has KNOWN hearing loss-associated genes, mutations and SNPs thereby effectively detecting if the person has known mutation and SNPs that are associated with hearing loss would have been obvious and did not require the teachings from the specification because Williamson teaches the genes. Therefore as set forth in the previous office action it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention was made to detect ANY AND ALL SNPs and other genetic aberrations known to be associated with human hearing loss as taught by Williamson. Guo teaches the high throughput array techniques for mutation detection in a cost effective efficient manner. Guo teaches to put many genes and SNPs known to be associated with a human phenotype altogether on an array for rapid and efficient detection method. Therefore the two references are combinable with a reasonable expectation of success, as the art is replete with guidance on how to construct arrays to detect specific SNPs, (See Guo) while Williamson teaches a large number of SNPs and genes that are associated with human hearing loss.

The response asserts, on page 7, para 2, that the list of hearing loss mutations in Williamson provides no prioritization to the importance or prevalence of these mutations

or genes in a population. One of ordinary skill in the art would not know, based on the generic list of genes provided in Williamson, to pick the specific genes and adjacent exons as claimed. Guo is silent as to any hearing loss gene, mutation or SNP. The combination of Williamson and Guo would require an undue amount of experimentation to select genes that would render a microarray or kit effective as a diagnostic hearing loss device.

This argument has been thoroughly reviewed but was not found persuasive. Williamson teaches mutations and genes and SNP and exons of a gene that are hearing loss associated. The list Williamson teaches is not a generic list but a specific list of genes, mutations, SNPs and exons of genes that are known to be associated with hearing loss. One of ordinary skill in the art would have been motivated to put all known genes and mutations including an exon-specific probes that are hearing loss-associated that Williamson teaches on an array for cost effective and high throughput analysis, simultaneously detecting multiple SNPs and genes and exons of genes associated with a human hearing loss. Guo teaches the high throughput array techniques for mutation detection in a cost effective efficient manner. Guo teaches to put genes and SNPs known to be associated with a human disease on an array for rapid and efficient detection method. Because Williamson teaches hearing loss-associated genes, mutations and exons of the genes, there is no undue experimentation to select the genes. One of ordinary skill in the art would have been motivated to put all the known genes and mutations Williamson teaches on an array in view of the hearing loss-associated genes and mutations taught by Williams. Therefore there is no undue

amount of experimentation to select genes that would render a microarray or a kit effective as a diagnostic hearing loss device, as exemplified by Guo who teaches how to construct arrays to known SNPs.

6. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Dan-Sung C. Cho whose telephone number is (571) 272-9933. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). The Central Fax Number for official correspondence is (571) 273-8300.

Dan-Sung C. Cho

JEHANNE SITTON
PRIMARY EXAMINER
5/29/07